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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/776,568	02/10/2004	Carolyn Petersen	PC25699A	2771

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EXAMINER	
WANG, LOUISE Z	
ART UNIT	**PAPER NUMBER**
1648	

DATE MAILED: 11/02/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/776,568	PETERSEN ET AL.	
	Examiner	Art Unit	
	Louise Wang	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 September 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-80* is/are pending in the application.

4a) Of the above claim(s) *75-80* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-74* is/are rejected.

7)☒ Claim(s) *74* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4/5/2004, 1/18/2005*
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Election/Restrictions

The Office acknowledges the receipt of Applicant's election filed on 7 September 2005. Applicant elects Group I, claims 1-74, without traverse.

Claims 1-80 are pending. Claims 75-80 are nonelected. Claims 1-74 are rejected.

Information Disclosure Statement

Initialed and dated copies of Applicant's IDS form 1449, filed 18 January 2005 and 5 April 2005, are attached to the instant Office action.

Claim Objections

Claim 74 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 71. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 22-24, 26, 41-48, 70, 72, and 73 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly

claim the subject matter which applicant regards as the invention. Regarding claims 22-24, 26, 41-48, 70, 72, and 73, the phrase "at least about" renders the claims indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(b).

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 9-13, 15-19, 30-38, 50, 54, and 59-67 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 9-13, 15-19, 30-38, 50, 54, and 59-67 are directed to a method for treating HIV in a mammal comprising administering nelfinavir or a pharmaceutically acceptable salt or solvate thereof with food comprising more than 50% fat by energy content.

The amount of guidance presented in the specification is limited to administering nelfinavir with food comprising 20% or 50% fat and 125, 500, or 1000 kcal of energy content in humans. There is insufficient evidence to demonstrate that those in the art would be able to use the method of co-administration of nelfinavir with food with more

than 50% fat, according to the claims, to treat HIV infection. Due to the complex and unpredictable nature of protease inhibitor metabolism, there is a large amount of undue experimentation necessary to address the many uncertainties commonly faced by those skilled in the art. In studies presented by Kurowski *et al.* and Lenhard *et al.* (IDS 05 April 2004), comparison of plasma drug concentrations in mammals after administration of nelfinavir with food showed no significant difference between administration with low fat food and with high fat food. Lenhard *et al.* further cautioned that experimental results from rodents should not be extrapolated to humans without analogous studies. Evidently, factors such as oral bioavailability, drug adherence, and metabolism may or may not be affected by the % fat and kcal of the food to be taken with nelfinavir. In view of the contradictory results from Kurowski *et al.* and Lenhard *et al.* and absent working examples and specific teachings, one cannot predict whether the co-administration of nelfinavir with food containing more than 50% fat would increase absorption of nelfinavir. Therefore, those in the art would not be able to treat HIV infection with the claimed invention.

Considering the lack of data or working examples in the specification, the state and nature of the art, and the teachings regarding unpredictability in this art, Applicant has not provided sufficient disclosure to enable those in the art to practice the claimed method in claims 9-13, 15-19, 30-38, 50, 54, and 59-67 without undue experimentation.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-23, 25-47, 49-72, and 74 are rejected under 35 U.S.C. 103(a) as being unpatentable over Maurice *et al* (STEP Perspective, 1997) in view of Regazzi *et al.* (Journal of Antimicrobial Chemotherapy, 2000) and Quart *et al.* (1995, reference in IDS filed on 05 April 2004).

Claims 1-24, 26-48, 50-70, 72, and 73 are directed to a method of treating human immunodeficiency virus (HIV) in a mammal comprising administering to the mammal a therapeutically effective amount of nelfinavir or a pharmaceutically acceptable salt or solvate thereof, wherein at least once daily the nelfinavir is administered with high-energy, high-fat food, wherein the mammal is not receiving ritonavir, saquinavir, or lopinavir, or a stereoisomer, solvate, salt, or prodrug thereof, and wherein the AUC after nelfinavir administration with food is at least about 3-fold greater than the AUC after administration in the fasted state.

Maurice *et al* teaches a regimen of nelfinavir taken three times a day with meals or a substantial snack to increase absorption into the blood. A substantial snack is differentiated from a very low fat snack containing less than 300 calories and 2 grams of fat, which is recommended for a different protease inhibitor, indinavir. Suggested food with nelfinavir include: cereal (110 kcal, 1.8 g fat) and milk (122 to 149 kcal, 3.1 to 8.1 g), tortilla (32 kcal, 3.5 g) with rice (361 kcal, 0.8 g fat) and beans (13 kcal, 2 g), bagel (5

kcal, 1 g), fig bars (18 kcal, 2g), juice (110 kcal, 0.1 g), sandwich (262 kcal, 29g), cheese and crackers (138 kcal, 16 g). According to the nutrition facts listed in the specification on page 14 to 15 and the data of one standard serving of each food item, it would be reasonable to one of ordinary skill in the art that the calculated energy content of different combinations of these suggested food meets the limitations of the % fat and kcal of the food recited in the instant invention.

Maurice *et al* does not teach the timeframe within which nelfinavir is administered in relation to food consumption. However, Maurice *et al* teaches the administration of indinavir one hour before a meal or two hours after a meal and the administration of saquinavir or ritonavir within two hours of a meal or snack. It would have been obvious to one of ordinary skill in the art to administer with the same schedule since indinavir, saquinavir, and ritonavir are in the same class of drugs, HIV protease inhibitors, as nelfinavir. The disclosed schedule for the administration of nelfinavir overlaps with the schedule recited in the instant invention.

Maurice *et al* does not teach the regimen restricting concurrent administration of ritonavir, saquinavir, or lopinavir, or a stereoisomer, solvate, salt, or prodrug thereof. However, Regazzi *et al.* teach a treatment of nelfinavir in combination therapy with efavirenz and stavudine (page 343). Regazzi *et al.* emphasize that the treatment study excludes patients with concurrent use of medications known to be inhibitors or inducers of cytochrome P450 3A (page 344), which include ritonavir, saquinavir or lopinavir or a stereoisomer, solvate, salt, or prodrug thereof.

Maurice *et al* does not teach the food effect on AUC values of nelfinavir. However, Quart *et al.* teach a food effect study of nelfinavir which resulted in AUC values after administration in fasted state that are 27-50% of those observed after administration in fed state. In other words, Quart *et al.* observed that AUC after nelfinavir administration with food is about 2 to 3.7-fold greater than the AUC after administration in the fasted state.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the nelfinavir treatment regimen of Maurice *et al.* to the instantly claimed regimen, as suggested by Regazzi *et al.* and Quart *et al.*, with a reasonable expectation of success. The motivation to do so is provided by Quart *et al.*, which shows the increase in plasma concentration in AUC values of nelfinavir as an effect of food taken with nelfinavir, the teaching of Regazzi *et al.* to exclude other protease inhibitors to be used together with nelfinavir, and food suggestions of Maurice *et al.* to take with nelfinavir.

Therefore, claims 1-23, 25-47, 49-72, and 74 are obvious over Maurice *et al.* in view of Regazzi *et al.* and Quart *et al.*

Remarks

No claims are allowed.

Claims 24, 48, and 73 are apparently free of the art of record. The closest prior art is Quart *et al*, which discloses a 27-50% difference in AUC between the

administration under fed and fasting conditions. However, Quart *et al* does not teach or suggest the claimed 5-fold increase in AUC for nelfinavir administration with food. Thus, Quart *et al.* is not applied to claims 24, 48, and 73.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Louise Wang whose telephone number is 571-272-5543. The examiner can normally be reached on Mon-Fri, 9am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Louise Wang, Ph.D.
25 October 2005

JEFFREY STUCKER
PRIMARY EXAMINER